16p11.2 Microdeletion and Prader Willi Syndrome (PWS) Similarities and Differences

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Introduction

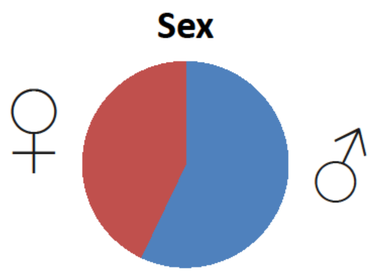
Prader Willi Syndrome is the most common syndromic form of obesity, caused by the absence of expression of the paternally active gens on the long arm of chromosome 15. Our hospital is a referral center for individuals with PWS in our area.
The 16p11.2 microdeletion has recently been recognized as a syndromic condition appearing to be a predisposing factor for overweight. This tendency has been identified in almost half of the children and adults with this deletion being the second most common genetic cause of obesity. One possible causative gen- SH2B1- involving leptin and insulin signaling, has been identified, although other genes may play a role.

Case report

We describe a case series of seven patients diagnosed with 16p11.2 deletion in our hospital between 2013-2015 and compare their main features with the pediatric population of SPW syndrome in our hospital (n= 26)

Four of them were men with an average age at diagnosis of 9.9±6.1 years. Two of them were referred to our clinical genetics department with a suspected diagnosis of PWS. The other five patients were referred because of developmental delay and two of them also suffered from seizures. Five of them had a sex-specific BMI for age over 95th percent. The mean length of deletion was 530.7Kb [448-598]. One patient, the oldest one (22 years) had sleep apnoea.

16p11.2 deletion (n= 7)

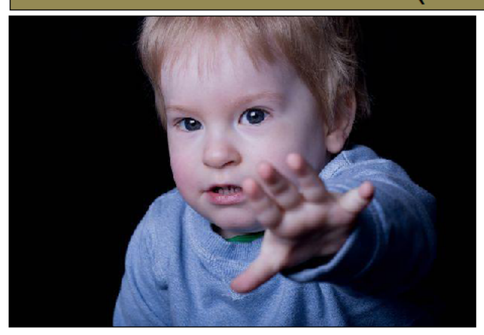


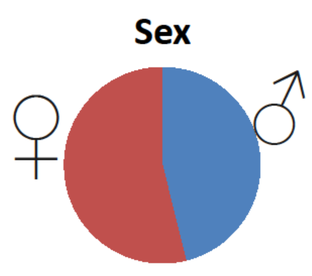
Age at diagnosis (years)	SD
9,9	6'1

Sex specific BMI for age	SD
0'94	2'2

Mean lenght of deletion	Range
530'7 Kb	[448-598]

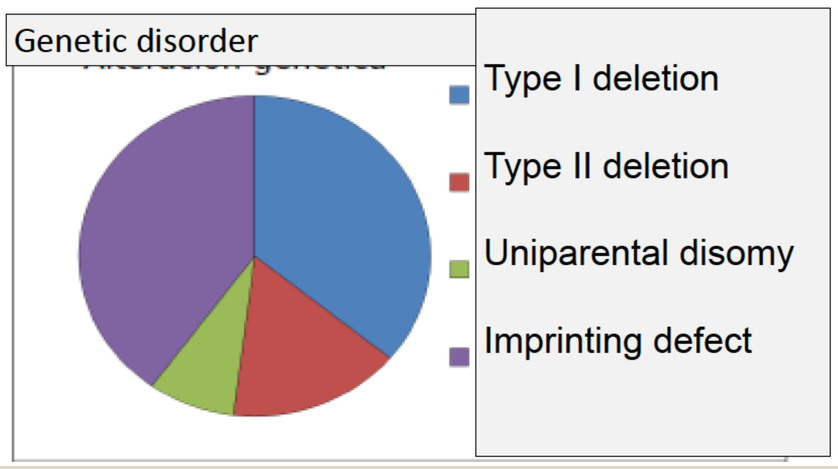
PWS (n =26)





Age at diagnosis (years)	SD
7'9	4'9

Sex specific BMI for age	SD
0'86	2'8



Males and females are equally affected in both diseases. In the same way as PWS individuals, patients with 16p11.2 deletion present with hypotonia at birth, causing feeding problems. They may exhibit developmental delay, intellectual disability, and/or autism spectrum disorder. Data suggest it also may contribute to psychiatric disease.
Weight is variable in childhood, but hyperphagia and obesity usually starts from one year on in PWS and later in 16p11.2 deletion. On the other hand, individuals with 16p11.2 syndrome don't have short stature (growth hormone deficiency) nor other hormonal deficiencies as PWS individuals do (thyroid or reproductive axis). They can suffer from minor cardiac malformations but not from scoliosis. They appear to be at higher than average risk for seizures or EEG abnormalities without overt seizures, based on a few retrospective clinical reports in which seizures were identified.

Conclusions

- Since the implementation of array analysis, numerous microdeletion syndromes as 16p11.2 have been described.
- Further research is needed for a comprehensive characterization of a genotype-phenotype correlation. No long term clinical follow up data are available.
- It should be considered as one of the genetic causes of obesity following Prader Willi Syndrome.
- It is important to identify clinical characteristics, leading to perform genetic testing and counseling.

Bibliography

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